Endovenous laser ablation of varicose veins with the 1470-nm diode laser

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Background: **Endovenous laser ablation (EVLA) is one of the most accepted treatment options for varicose veins. In previous studies conducted with a laser at 810 to 1320 nm, paresthesia, pain, and ecchymosis were common adverse effects. We hypothesized that a lower linear endovenous energy density (LEED), as used with 1470-nm diode laser fibers, would lead to a reduction in adverse events.**

Methods: **We conducted a prospective, nonrandomized observational cohort study of 312 consecutively treated lower limbs legs in 286 patients. Of these, a bare laser fiber (ELVeS-plus kit) was used to treat 168 legs in 150 patients (group 1), and a radial fiber (ELVeS-radial kit) was used in 144 legs in 136 patients (group 2). Laser treatment was performed in the great saphenous vein. Follow-up for all patients was 3 months. The primary end point was the occurrence of ecchymosis and bruising. This was correlated to the reduced LEED needed with the 1470-nm diode laser.**

Results: **Laser fiber (odds ratio [OR], 22.3; 95% confidence interval [CI], 20.2-24.5) and body mass index (OR, 0.35; 95% CI, 0.15-0.55) were identified as independent parameters for LEED. In group 2 compared with group 1, LEED in the great saphenous vein could be reduced from 79.4 ± 9.1 to 57.4 ± 10 J/cm ($P < .0001$). LEED was an independent parameter for skin bleeding (OR, 1.04; 95% CI, 1.017-1.058). Ecchymosis and bruising were significantly less frequent in group 2 than in group 1 ($P < .0001$). The need for analgesia was low, with 103.08 ± 15.34 mg diclofenac-sodium in group 1 vs 82.08 ± 18.86 mg in group 2 ($P < .04$). Occlusion with elimination of reflux was achieved in 100% of group 1 and group 2 ($P < 1$). No recanalization occurred at follow-up.**

Conclusion: **Endovenous laser treatment of varicose veins in the great saphenous vein with the 1470-nm diode laser is safe and highly effective. The lower energy level needed using the radial laser fiber significantly minimized adverse effects compared with the bare laser fiber. (J Vasc Surg 2010;51:1474-8.)**

Varicose veins are a common disease in Western countries, with a prevalence of up to 20% in men and >25% in women.[1] In the last decade, the spectrum of treatment for varicose veins has been broadened. New, less invasive treatment options than surgery have been introduced, such as ultrasound-guided foam sclerotherapy, radiofrequency ablation, and endovenous laser ablation (EVLA). The first report on EVLA was published in 1999.[2] Several studies have since been published reporting different regimens for the energy per surface area (J/cm), pulse duration, and wavelength of the laser. The published data on efficacy and safety of laser treatment arise from a laser with a wavelength between 810 and 1320 nm and show 90% to 100% occlusion.[3-7]

A new-generation laser with a longer wavelength of 1470 nm was recently introduced. Some have hypothesized that efficacy would be higher due to higher specificity for the interstitial water in the vessel wall of this laser and lower absorption by hemoglobin[7-9]; however, data are scarce. We assessed the efficacy and safety of the new laser with 1470-nm wavelength in a prospective study in consecutive patients and compared efficacy and safety of the 1470-nm bare fiber vs the 1470-nm radial laser fiber. We also studied the lower linear endovenous energy density (LEED) used with the different 1470-nm laser fibers and its correlation to the observed postinterventional skin bleeding.

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Competition of interest: none.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a competition of interest.

0741-5214/$36.00

doi:10.1016/j.jvs.2010.01.027

METHODS

Patients. Our prospective, nonrandomized study included consecutive patients who underwent EVLA of incompetent varicose veins. All patients who presented at our vascular diagnostics unit were referred by their general practitioners for symptoms suggestive of symptomatic varicose veins. All patients gave informed consent for the procedure. The study protocol was approved by the institutional ethics committee of the University of Freiburg Medical School.

All patients were seen by a vascular physician who specialized in venous disease. The baseline examination included history, physical examination, and venous duplex ultrasound imaging of the lower extremity veins. Inclusion criteria for the study were varicose veins with ultrasound-documented reflux in the great saphenous vein (GSV) judged suitable for endovenous treatment. We excluded patients from EVLA treatment if the average size of the varicose vein was >2 cm or if there was extreme tortuosity.

Examinations and procedures. Venous ultrasound imaging was performed at each presentation (HDI 5000, linear array, 4-7 MHz [ATL, Bothell, Wash] and zone

(linear array 8-3 MHz [ZONARE, Mountain View, Calif]) using a standardized examination protocol.[10,11] The veins were examined with the patient upright to determine venous reflux, defined as retrograde flow of >0.5-second duration.[12] The CEAP classification of varicose veins was determined for all patients.[13,14]

The bare and radial fibers that were used in this study are suitable for the 1470-nm diode laser (Cerelas D, Biolitec). The 600 μm ELVeS-plus kit consists of a bare fiber, a guiding catheter of 70 cm or 100 cm length with guidance markings for cm or controlled pull-back, a 5 Fr sheath, a 0.035 J tip guide wire with length of 150 cm, and a 19G × 7cm entry needle. The ELVeS-radial kit consists of a 600 μm radial fiber with guidance markings, a 6 Fr sheath with 12 cm introducer length, a 0.0038 J-tip guide wire with 45 cm length, and a 19G × 7 cm entry needle. The bare fiber releases its energy only in a straight, forward direction, whereas the energy from the radial fiber is emitted in a 360° manner from a nontraumatic fiber tip. Laser treatment started while a second venous ultrasound imaging study was performed of the area of treatment. The entire procedure was guided by venous ultrasound imaging.

The varicose vein was punctured at the distal insufficiency point. The entry of the varicose vein into the deep vein was controlled by ultrasound guidance. The placement of the laser fibers was performed according to the manufacturer's guidelines.

A tumescent local anesthesia was given consisting of 25 mL of 2% Ultracaine (Sanofi-Aventis, Frankfurt, Germany), 25 mL of sodium carbonate, and 0.5 mL of epinephrine diluted in 500 mL of cooled saline along the perivenous space with the use of ultrasound guidance. Laser energy was delivered at 15 W using the bare fiber and 10 W using the radial fiber. The varicose vein was treated to approximately 1 cm above the skin entry site. LEED (J/cm), a surrogate marker of fluence (J/cm^2), was calculated as described elsewhere.[15,16] The applied laser energy was 100 J/cm for the bare fiber vs 80 J/cm for the radial fiber at the proximal 10 cm above the knee, 80 vs 60 J/cm at the following length above the knee, and 60 J/cm for both fibers below the knee. Laser energy application was controlled, modifying the velocity until withdrawal of the catheter. To control pullback we used in both groups catheter equipped with a ruler. In the area of the saphenofemoral junction the catheter was placed on the level of the inflow of the inferior superficial epigastric vein. After the procedure, venous outflow was checked immediately in the proximal deep veins by ultrasound imaging. Persistent reflux in tributaries or below the treated vein was checked, and additional treatment with foam sclerotherapy was applied if needed.

Immediately after the procedure, prophylaxis of venous thromboembolism with subcutaneous enoxaparin (40 mg) was started and continued for the next 5 days.

Compression therapy with a graduated class II stocking at 30 to 40 mm Hg was initiated immediately. Patients were to wear the stockings for 24 hours for 1 week, then during the day for a further 3 weeks. Diclofenac sodium, a nonsteroidal anti-inflammatory drug was prescribed (75 mg, 3 to 5 days, twice daily) for optional use. The patient was told to resume routine daily activities but to avoid strenuous exercise for about 1 week.

Follow-up examinations were performed at 1 week, 1 month, and 3 months after laser therapy and included clinical examination and venous ultrasound imaging of the treated leg. Any clinical sign of hematoma or ecchymosis was noted and summarized as skin bleeding. Signs for phlebitis were also checked.

The aim of the ultrasound imaging was to examine the treated vein and the surrounding area for venous reflux and the treated vein for recanalization and also to exclude deep vein thrombosis (DVT) in the leg. All patients were requested to present in our vascular unit or contact us by phone if symptoms of DVT or pulmonary embolism (PE) developed. The diagnostic criterion for thrombosis was the lack of compressibility of 1 or more segments of the veins of the lower extremity. We treated DVT and PE according to standard protocols. We also asked for the amount of pain relief medication required after the procedure.

Study end points. The primary study end point was the occurrence of ecchymosis, bruising, and the reduction of LEED. The primary efficacy end point was ultrasound-proven elimination of venous reflux in a treated varicose vein by laser after 3 months. Secondary efficacy and further safety end points after 3 months were: (1) ultrasound-proven occlusion of the treated vein (2) and exclusion of recanalization of the treated vein segments; (3) DVT, superficial vein thrombosis (SVT), or clinical PE, as defined by objective testing; (4) death from any cause; and (5) clinical complaints during procedure, such as pain, and paresthesia.

Statistical analysis. Differences between the study groups were noted by analysis of variance, χ^2 test, and Fisher's exact test, as appropriate. Values of $P < .05$ were considered significant. A logistic regression analysis was used to assess the risk for skin bleeding events in the study groups adjusted for sex, age, body mass index, LEED, and treated leg. Results of the regression model are given as odds ratio (OR) and 95% confidence intervals (CI). To identify factors that correlate with LEED, we performed a multivariable analysis using the general linear model. As independent variables, this multivariable model included age, sex, body mass index, treated side and laser fiber. Calculations were performed with SPSS 11.5 software (SPSS, Chicago, Ill).

RESULTS

Patients. From August 2007 until May 2009, we treated 312 legs in 286 patients with the 1470-nm diode laser. Energy was delivered intraluminally. Between August 2007 and October 2008, we used the bare fiber in 168 legs in 150 patients (group 1), and between November 2008 and May 2009, we used the radial fiber in 144 legs in 136 patients (group 2). Procedures in patients who required bilateral treatment were performed at different sessions with a time interval >4 weeks.

Table I. Patient characteristics according to limb treatment by bare or radial fiber

Variable	*Bare fiber*	*Radial fiber*	P
Patients, No.	168	144	
Sex			
Male	57	41	
Female	112	103	.3
Age, y			
Mean ± SD	61 ± 13.8	57 ± 13.9	.005
Range	16-88	23-85	
BMI, kg/m^2			
Mean ± SD	26.5 ± 6.33	26.3 ± 4.67	.8
Range	17.3-56.2	18.5-45.9	
Treated side			
Right	89	71	.7
Left	79	73	
CEAP, No. (%)			
C_2	100 (59.5)	84 (58.3)	.9
C_3	22 (13.1)	29 (20.1)	.09
C_4	31 (18.5)	25 (17.4)	.8
C_5	3 (1.8)	3 (2.1)	.9
C_6	12 (7.1)	3 (2.1)	.06

BMI, Body mass index; *SD,* standard deviation.

Table II. A, Multivariate analysis for linear endovenous energy density

Variable	*Adjusted difference (95% CI)*	P
Age, years	0.003 (−0.079 to 0.085)	.946
Sex, M/F	−0.547 (−2.867 to 1.772)	.643
Side, R/L	−2.306 (−4.423 to −0.188)	.033
BMI, kg/m^2	0.349 (0.146 to 0.551)	.001
Laser fiber[a]	22.331 (20.167 to 24.496)	.0001

BMI, Body mass index; *CI,* confidence interval.
[a]Bare fiber vs radial fiber.

Table II. B, Regression analysis for risk of skin bleeding

Variable	*OR (95% CI)*	P
LEED	1.037 (1.017 to 1.058)	.0001
Age, years	0.982 (0.962 to 1.004)	.105
Sex, M/F	0.760 (0.421 to 1.371)	.362
Side, R/L	0.799 (0.460 to 1.389)	.427
BMI	1.013 (0.960 to 1.068)	.648

BMI, Body mass index; *CI,* confidence interval; *LEED,* linear endovenous energy density; *OR,* odds ratio.

Table III. Intervention according to limb treatment with bare or radial fiber

Variable	*Bare fiber*	*Radial fiber*	P
Patients, No.	168	144	
Combined treatment,[a] No. (%)	102 (60.7)	108 (75.0)	.02
Operation time, min			
Mean ± SD	46.85 ± 11.39	45.72 ± 12.63	.39
Range	20-120	15-75	
LEED GSV J/cm			
Mean ± SD	79.4 ± 9.1	57.4 ± 10.0	.0001
Range	48.5-118.3	15.4-89.3	

GSV, Great saphenous vein; *LEED,* linear endovenous energy density; *SD,* standard deviation.
[a]Laser plus foam sclerotherapy.

The baseline characteristics of the two study groups are reported in Table I. The group 2 patients were significantly younger than group 1 patients.

Four patients in group 1 (4 limbs, 2.38%) were lost to the 3-month follow-up evaluation due to patient refusal. In group 2, 3-month follow-up data were missing in eight patients (8 limbs/5.55%) owing to one death and seven refusals. All patients lost to follow-up were contacted by phone. The reason not to present in our unit was due to a long distance between the patient and our hospital – and due to lack of complaints. Thus, the 3-month follow-up data could be completed in 300 of 312 limbs (96.2%).

Endovenous procedure. The total average time of the procedure, beginning with the initial ultrasound imaging until leaving the examination table was 46.85 ± 11.39 minutes in group 1 and 45.72 ± 12.63 minutes in group 2, which was not significant. Delivery of LEED was significantly lower in group 2 in laser treatments of the GSV (57.4 vs 79.4 J/cm group 1; $P < .0001$). As independent parameters for LEED, we could identify laser fiber (OR, 22.3; 95% CI, 20.17-24.49), and body mass index (OR 0.35, 95% CI, 0.15-0.55). Compared with group 1, LEED in the GSV in group 2 could be reduced from 79.4 ± 9.1 to 57.4 ± 10 J/cm ($P < .0001$; Table II). All results are given in Table III.

Safety outcomes. Any skin bleeding was seen significantly less frequently in group 2 than in group 1 ($P < .0001$; Table II). Skin bleeding in group 2 were mostly puncture-related after applying tumescent anesthesia or after introducing the 6F sheath. In group 1, large areas of skin bleeding were frequently seen around the treated area. No hematoma could be detected in all sonographical examinations in both groups. All bleeding-related skin alterations disappeared completely in both groups after 3 months. LEED was an independent parameter for skin bleeding (OR, 1.04; 95% CI, 1.017-1.058).

We used ultrasound imaging to diagnose postprocedural DVT in two patients in group 1 (1.30%), comprising an ascending asymptomatic thrombosis with extension into the common femoral vein in a 29-year-old woman after 1 week and a symptomatic femoral thrombosis with proven PE in a 50-year-old obese woman (BMI, 56.15 kg/m^2) at 28 days. The latter patient showed no sign of venous thromboembolism at the 1-week follow-up. All patients with DVT were treated successfully after an initial treatment with full-dose anticoagulation therapy. No venous thromboembolism occurred in group 2.

Superficial vein thrombosis (SVT) was diagnosed in three patients in each group (1.9%). SVT was seen distally to the treated segments or in tributaries of the thigh with hampered or blocked outflow.

Table IV. Outcome at 3-month follow-up evaluation according to limb treatment by bare or radial fiber

	Bare fiber	*Radial fiber*	P *value*
Patients, No.	168	144	.5
Deaths ≤3 months, No. (%)	0 (0%)	1 (0.7%)	
3-month results, No. (%)			
Occlusion	168 (100)	144 (100)	>.99
Side effects, No. (%)			
Deep vein thrombosis	2 (1.2)	0 (0)	.5
Pulmonary embolism	1 (0,6)	0 (0)	.6
Phlebitis	3 (1.8)	3 (2.1)	.8
Paresthesia	0 (0)	0 (0)	>.99
Ecchymoses, hematoma	141 (83.9)	92 (63.9)	.0001
Analgesia use,[a] mean ± SD, mg	103.08 ± 15.34	82.08 ± 18.86	.04
No need for analgesia, No. (%)	36 (21.4)	51 (35.4)	

SD, standard deviation.
[a]Diclofenac sodium.

No group 1 patients died during 3 months of follow-up. One patient in group 2 died of ventricular fibrillation not related to the procedure.

Pain relief medication was significantly lower in group 2 (82.08 ± 18.86 mg vs 103.08 ± 15.34 mg of diclofenac sodium, $P < .04$). All outcomes of both study groups are reported in Table IV.

Efficacy outcomes. The primary efficacy end point of our study did not differ significantly between the two groups. In group 1, we achieved elimination of venous reflux and immediate occlusion in 168 of 168 limbs (100%) after one laser procedure. Elimination of reflux occurred after the second procedure in one patient with a vein diameter of 2 cm. In group 2, elimination of reflux was achieved in all treated limbs as well (100% occlusion). In both groups, no recanalization of the treated vein was diagnosed with ultrasound imaging during follow-up. After 3 months, all venous ulcers were sealed in both groups (14 total: 12 in group 1 and 2 in group 2).

DISCUSSION

The aim of endovenous procedures is to establish a less invasive, highly effective, and safe therapeutic option in the treatment of varicose veins compared with surgery. The efficacy results of our study show superiority of the 1470-nm diode laser to most published data obtained with an 810- to 980-nm diode laser, in which energy is known to be absorbed by deoxygenated hemoglobin.[8] The recently introduced 1470-nm laser acts directly on the vessel wall through the absorption by the interstitial water. In addition, the lately developed radial fiber emits light at 360°, causing a homogenous alteration of the vein wall. These direct effects induce complete occlusion of the vein in approximately 100% of the treated vein segments and thereby eliminate venous reflux.

In endovenous procedures, the amount of energy applied on a vessel segment depends on the wattage (J/s) and the duration of treatment. The amount of energy given was an independent predictor of vessel occlusion.[16] It was reported that 80 J/cm is required to gain treatment success.[17,18] These results, however, concerned the hemoglobin-specific laser wavelength. Our results with the water-specific 1470-nm laser show that in both groups, LEED could be further reduced without loss of efficacy.

Comparison of bare and radial laser fibers. Our results show no statistically significant differences in efficacy between the treatment groups. With regard to procedure safety, treatment with the radial fiber showed significantly less skin bleeding events and necessitated less pain relief. In group 2 in our study compared with other studies, LEED was much lower, with a mean of 58.94 J/cm for GSV.

Pannier et al,[19] who published the first data on 100 patients treated with a 1470-nm diode laser, demonstrated a 100% occlusion rate after 1 year, but their drop-out rate of 17% was quite high.[19] They treated the patients with a bare fiber, as in group 1 of our study. In the Pannier et al study, mean LEED was 107 J/cm for GSV. Safety results in their study showed a paresthesia rate in the treated area of 9.5% persisting after 6 months and 7.6% after 1 year.[19] They suggested a correlation between LEED and patient discomfort.

In our study, the lower incidence of side effects, such as skin bleeding in the radial fiber group, demonstrates a correlation with the lower energy applied. This was also reflected in the lower need for analgesia in the radial fiber group. The lower incidence of adverse events with the radial fiber is probably because perforation of the vein is very unlikely. This is suggested by a study using an ex vivo model in a cow's foot.[20]

Study limitations. We present a short-term follow-up of 3 months, during which time no recanalization occurred of treated varicose veins. Thus, the long-term success compared with other treatment options, such as surgery, remains to be assessed by future studies.

Another limitation is the nonrandomized nature of our study, which resulted in differences in baseline characteristics between the two groups, particularly with respect to the type of veins treated. Nevertheless, a correlation of a lower, but still highly effective LEED, and the statistically significant reduction of side effects prevailed even after stratification for the type of vein treated.

CONCLUSION

We demonstrate that treatment of varicose veins with 1470-nm endovenous laser therapy is safe and effective. Compared with the bare fiber, the radial fiber reduces the energy requirement, adverse side effects, and patient discomfort at a comparable success rate. Thus, for future studies of the long-term outcome of endovenous proce-

dures compared with surgery, the 1470-nm endovenous laser combined with radial fiber appears to be the most promising device.

AUTHOR CONTRIBUTIONS

Conception and design: TS
Analysis and interpretation: TS, EH, CF
Data collection: TS, CV
Writing the article: TS
Critical revision of the article: TS, TZ, FN
Final approval of the article: TS, EH, CF, AR, TZ, FN
Statistical analysis: AR
Obtained funding: Not applicable
Overall responsibility: TS

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Submitted Nov 12, 2009, accepted Jan 7, 2010.